

**AMENDMENT IN RESPONSE TO OFFICE ACTION**  
**U.S. Application Serial N . 09/582,592**

**REMARKS**

Applicant has amended claims 4 and 5 to correct some obvious typographical errors, changing "CL" to "Cl" and "NA" to "Na". In addition, claims 4 and 5 have been amended to further distinguish over the prior art.

Claims 3-5 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Cushman (US Patent No. 5,430,062) or Pettit (US Patent 4,996,237). This rejection has been carefully considered, and is respectfully traversed, for the reasons discussed below.

The presently claimed invention relates to antineoplastic compounds and water soluble prodrugs thereof. The phenstatins as presently claimed belong to the benzophenone series of compounds, whereas in contrast the combretastatins disclosed by Pettit '237 are stilbenes; Cushman '062 discloses certain stilbene derivatives for use as anticancer agents. One of ordinary skill in the relevant art at the time the presently claimed invention was made would have found nothing in either of the cited references to suggest the presently claimed compounds and method. In fact, the present inventors' discovery that phenstatin has anti-cancer activity was quite by chance.

The Office Action urges that Cushman '062 discloses phenstatin compounds and derivatives similar to those presently claims, and points in particular to columns 19 and 20. Cushman does not disclose or suggest modifying the compounds it discloses to arrive at the particularly defined prodrugs set forth in the instant claims. It should be added that according to the National Institutes of Health (NIH), no certainty (and hence no obviousness) exists where the treatment of neoplastic disease is concerned. In fact, structural similarity between compounds does not mean that the compounds will be similarly active, nor does it mean that the compounds will be the same in terms of efficacy, safety, administration, etc. Neither reference discloses or otherwise teaches how to modify the compounds to arrive at the prodrugs as presently claimed;

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the prodrugs as claimed provide good solubility, which permits the claimed prodrugs to be easily administered. The cited references simply do not teach the instantly claimed prodrug compounds.

The Patent Office is respectfully requested to advise why one of ordinary skill in the art would be motivated to modify the compounds disclosed therein to arrive at the presently claimed prodrugs.

Applicant submits that the claims now present are in full compliance with 35 U.S.C. § 112. Applicant therefore requests reconsideration and allowance of all of the claims in the application. The Examiner is invited to telephone the Applicant's undersigned representative, if this would in any way facilitate prosecution of the application.

Dated: Sep 5, 2002

Respectfully submitted,



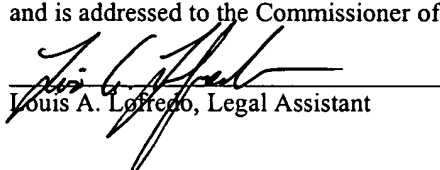
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**CERTIFICATE OF MAILING PURSUANT TO 37 C.F.R. § 1.10**

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Date of Deposit : September 5, 2002

I hereby certify that this paper and all documents and any fee referred to herein are being deposited on the date indicated above with the U.S. Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10, and is addressed to the Commissioner of Patents, U.S. Patent and Trademark Office, Washington, D.C. 20231.

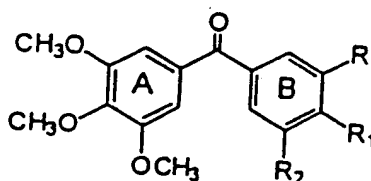
  
Louis A. Lofredo, Legal Assistant

9-5-2002  
Date of Signature

Version With Markings To Show Changes Made

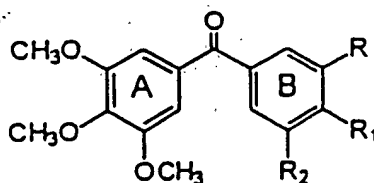
In the Claims

4. (Amended) Phenstatin prodrugs and derivatives thereof having the structure:



wherein when R=H and R<sub>1</sub> = OCH<sub>3</sub>, R<sub>2</sub> is OPO<sub>3</sub>Na<sub>2</sub> [OPO<sub>3</sub>NA<sub>2</sub>], OCOCH<sub>3</sub>, [H,<sub>1</sub>] or OCH<sub>3</sub>, and when R=R<sub>2</sub>, R<sub>2</sub> is OCH<sub>3</sub>, CH<sub>3</sub>, Cl [CL] or F and R<sub>1</sub> is H and when R<sub>1</sub>= R<sub>2</sub>, R<sub>2</sub> is OCH<sub>3</sub> or OCH<sub>2</sub>O and R is H.

5. (Amended) The method of inhibiting human cancer cell growth in a host inflicted therewith comprising administering to said host in a pharmaceutically acceptable carrier a small but effective amount of a compound selected from the group consisting of phenstatin, phenstatin prodrug and the derivatives thereof having the structure[.]



wherein when R=H and R<sub>1</sub>=OCH<sub>3</sub>, R<sub>2</sub> is OPO<sub>3</sub>Na<sub>2</sub> [OPO<sub>3</sub>NA<sub>2</sub>], OCOCH<sub>3</sub>, [H,<sub>1</sub>] or OCH<sub>3</sub>, and when R=R<sub>2</sub>, R<sub>2</sub> is OCH<sub>3</sub>, CH<sub>3</sub>, Cl [CL] or F and R<sub>1</sub> is H and when R<sub>1</sub>= R<sub>2</sub>, R<sub>2</sub> is OCH<sub>3</sub> or OCH<sub>2</sub>O and R is H.